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EXAMINER

SAJJADI, FEREDYDOUN GHOTB

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/577,840	<b>Applicant(s)</b> CARDONA IGLESIAS ET AL.	
	<b>Examiner</b> FEREYDOUN G. SAJJADI	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 23 December 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 13-60 is/are pending in the application.
- 4a) Of the above claim(s) 13-19, 21-27, 35-37 and 44-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20, 28-34, 38-43 and 47-60 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/1/2006; 12/23/2008</u> .                                    | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This action is in response to papers filed December 23, 2008. Applicants' response to the restriction requirement of September 24, 2008 has been entered. Claims 47-60 have been newly added. No claims were amended or cancelled. Currently, claims 13-60 are pending in the Application.

#### ***Election/Restrictions***

Applicants' election of Group II (claims 28-34, 38-43), drawn to a lyophilized immunotherapeutic agent and a pharmaceutical agent that contain cell wall fragments from a virulent *Mycobacterium tuberculosis*-complex (MTB-C) strain of cells, is acknowledged. The election was made with traverse. Applicants' species election of H37Rv as the species of MTB-C strain, octylphenol ethoxylate having 7-8 mol of ethylene oxide as the species of non-ionic surfactant and phosphatidylcholine as the species of liposome auxiliary lipid, is further acknowledged.

Applicants' traversal of the Group restriction is on the grounds that claim 20 should be assigned to Group II. Applicants' arguments are found persuasive, as claim 20 was incorrectly treated as a method claim by oversight. Accordingly, claim 20 is hereby rejoined with Group II claims.

The election requirement is deemed proper and is therefore made **FINAL**. Claims 13-19, 21-27, 35-37 and 44-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Elected claims have been examined commensurate in scope with the elected invention, and the elected species of the invention. Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Elected claims 20, 28-34, 38-43 and 47-60 are under current examination.

### ***Information Disclosure Statement***

The information disclosure statements (IDS) submitted on May 1, 2006 and December 23, 2008 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner, and indicated as such on Applicants' IDS form.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20, 28, 29, 38, and 47-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andersen et al. (U.S. Patent Application Publication No.: 2002/0094336; filed Feb. 20, 2001; of record), in view of Chatuverdi et al. (Vaccine 17:2882-2887; 1999).

The claims embrace an immunotherapeutic agent containing cell wall fragments from a virulent *Mycobacterium tuberculosis* H37Rv strain of cells and a pharmaceutical composition comprising the same.

Applicants have acknowledged that the immunotherapeutic agent in claim 20 is claimed as product by process claim, that reads on a homogenate of cells comprising non-fragmented cells and cell wall fragments. As non-fragmented cells include virulent H37Rv, such would not be considered immunotherapeutic. Claim 20 has therefore been examined to the extent that that the agent encompasses cell wall fragments of the H37Rv strain.

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MPEP 2112.01 states: “Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).”

MPEP 2113 further states: “[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Andersen et al. describe immunologically active peptide fragments of *M. tuberculosis* that may be used as compositions such as vaccines (Title and Abstract). The authors state that recombinant polypeptides may be isolated from whole bacteria of the tuberculosis complex for from lysates or fractions thereof, e.g. cell wall containing fractions (paragraph [0078], p. 9). Andersen et al. further state that in order to find new *M. tuberculosis* specific antigens for a new vaccine against TB, various ORF regions of *M. tuberculosis* H37Rv has been analyzed, as these regions are deleted from known BCG strains (paragraph [0175], p. 17. Andersen et al. further state that the vaccine comprising the immunogenic polypeptides may be prepared as a pharmaceutically acceptable ingredient containing auxiliary substances such as emulsifying and buffering agents (paragraph [0097], p. 11). Preparation of proteins in PBS buffer is described in Example 3, paragraph [0214], limitation of claim 52).

While Andersen et al. do not describe the preparation of Mycobacterial cell wall fragments, such was known in the prior art.

Chaturvedi et al. describe the preparation of protective antigens from the cell wall of *Mycobacterium habana* (Title and Abstract), by sonication, differential centrifugation, phase separation using Triton X-114, centrifugation, backwashing in buffer having a neutral pH, and recovery of protein fractions by precipitation and lyophilization (sections 2.1 and 2.3 p. 2883; limitation of claims 28 and 51). The authors present results from cell wall fraction vaccination

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against *M. tuberculosis* H37Rv, and state that the strain is a good choice as a candidate vaccine for tuberculosis (first column, p. 2887).

The teachings of Andersen et al. and Chaturvedi et al. are directed to the production of Mycobacterial protein vaccines. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine their respective teachings and to isolate cell wall fragments from the H37Rv strain for producing a vaccine composition, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to isolate cell wall fragments and formulate the same as a pharmaceutical vaccine composition, because Anderson et al. specifically teach pharmaceutical vaccine compositions of H37Rv strain proteins.

Claims 28-33, 38-42, 47, 54 and 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andersen et al. (U.S. Patent Application Publication No.: 2002/0094336; filed Feb. 20, 2001; of record), in view of Chatuverdi et al. (Vaccine 17:2882-2887; 1999), as applied to claims 20, 28, 29, 38, and 47-55 above, and further in view of Unger et al. (U.S. Patent No.: 6,443,898; filed June 7, 1995).

The claims embrace an immunotherapeutic agent containing cell wall fragments from a virulent *Mycobacterium tuberculosis* H37Rv strain of cells and a pharmaceutical composition comprising the same in the form or liposomes.

Andersen et al. describe immunologically active peptide fragments of *M. tuberculosis* that may be used as compositions such as vaccines (Title and Abstract). Andersen et al. further state that in order to find new *M. tuberculosis* specific antigens for a new vaccine against TB, various ORF regions of *M. tuberculosis* H37Rv has been analyzed, as these regions are deleted from known BCG strains (paragraph [0175], p. 17. Andersen et al. further state that the vaccine comprising the immunogenic polypeptides may be prepared as a pharmaceutically acceptable ingredient containing auxiliary substances such as emulsifying and buffering agents (paragraph [0097], p. 11).

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Chaturvedi et al. describe the preparation of protective antigens from the cell wall of *Mycobacterium habana* (Title and Abstract), by sonication, differential centrifugation, phase separation using Triton X-114, centrifugation, backwashing in buffer having a neutral pH, and recovery of protein fractions by precipitation and lyophilization (sections 2.1 and 2.3 p. 2883; limitation of claims 28 and 51). The authors present results from cell wall fraction vaccination against *M. tuberculosis* H37Rv, and state that the strain is a good choice as a candidate vaccine for tuberculosis (first column, p. 2887).

While Chaturvedi et al. do not describe the preparation of their Mycobacterial cell wall fragments a part of a liposome, such was known in the prior art.

Unger et al. describe therapeutic delivery systems comprising liposomes having encapsulated therein drugs (Abstract). Unger et al further describe various suitable therapeutics that include bacterial vaccines, microbial cell wall components and subunits of Mycobacteria (paragraph 91). Unger et al. state that dipalmitoyl-phosphatidylcholine may be included in the emulsification process to produce the liposomes (paragraph 11, 52 and 68), further disclosing phospholipid liposomes having a cholesterol coating (paragraphs 12, 13 and 79). Combinations of phosphatidylcholine and cholesterol are disclosed in paragraph 211.

The teachings of Andersen et al. Chaturvedi et al. and Unger et al. are directed to the production of Mycobacterial protein vaccines. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine their respective teachings and to produce cell wall fragments from the H37Rv strain encapsidated in liposomes as a vaccine composition, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to utilize the cell wall components as a liposomal pharmaceutical vaccine composition, because Unger et al. specifically teach the same.

Claims 28, 38, 39, 43, 47, 54 and 56-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andersen et al. (U.S. Patent Application Publication No.: 2002/0094336; filed Feb. 20, 2001; of record), in view of Chaturvedi et al. (Vaccine 17:2882-2887; 1999), and further

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in view of Unger et al. (U.S. Patent No.: 6,443,898; filed June 7, 1995) as applied to claims 28-33, 38-42, 47, 54 and 56-59 above, and Parikh I. (U.S. Patent No.: 5,785,975; Jul. 28, 1998).

The claims embrace an immunotherapeutic agent containing cell wall fragments from a virulent *Mycobacterium tuberculosis* H37Rv strain of cells and a pharmaceutical composition comprising the same in the form of liposomes, further comprising vitamin E.

Andersen et al. describe immunologically active peptide fragments of *M. tuberculosis* that may be used as compositions such as vaccines (Title and Abstract). Andersen et al. further state that in order to find new *M. tuberculosis* specific antigens for a new vaccine against TB, various ORF regions of *M. tuberculosis* H37Rv has been analyzed, as these regions are deleted from known BCG strains (paragraph [0175], p. 17).

Chaturvedi et al. describe the preparation of protective antigens from the cell wall of *Mycobacterium habana* (Title and Abstract), by sonication, differential centrifugation, phase separation using Triton X-114, centrifugation, backwashing in buffer having a neutral pH, and recovery of protein fractions by precipitation and lyophilization (sections 2.1 and 2.3 p. 2883; limitation of claims 28 and 51).

Unger et al. describe therapeutic delivery systems comprising liposomes having encapsulated therein drugs (Abstract). Unger et al further describe various suitable therapeutics that include bacterial vaccines, microbial cell wall components and subunits of Mycobacteria (paragraph 91).

While Unger et al. do not describe their liposome delivery system as comprising vitamin E, such was known in the prior art.

Parikh describes phospholipid adjuvant compositions and vaccine formulations (Abstract), stating that examples of vehicles with adjuvant-like activities include water/oil emulsions, oil/water emulsions, microencapsulation, and liposomes (paragraph 15), and in Example II, disclose a vaccine emulsion formulation comprising a mixture of .beta.-glucan-phospholipid conjugate, phosphatidylcholine and vitamin E (paragraph 44).

The teachings of Andersen et al. Chaturvedi et al. Unger et al. and Parikh are directed to the production of vaccines formulations. Therefore, it would have been *prima facie* obvious for a

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person of ordinary skill in the art, to combine their respective teachings and to produce cell wall fragments from the H37Rv strain encapsidated in liposomes as a vaccine composition further comprising vitamin E, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to include vitamin E as a liposomal pharmaceutical vaccine composition, because Parikh specifically teaches the same.

### ***Conclusion***

**Claims 20, 28-34, 38-43 and 47-60 are not allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/  
Examiner, Art Unit 1633